Engineered hydrogels increase the post-transplantation survival of encapsulated hESC-derived midbrain dopaminergic neurons.

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Public Summary:
Cell replacement therapies have broad biomedical potential; however, low cell survival and poor functional integration post-transplantation are major hurdles that hamper clinical benefit. For example, following striatal transplantation of midbrain dopaminergic (mDA) neurons for the treatment of Parkinson's disease (PD), only 1-5% of the neurons typically survive in preclinical models and in clinical trials. In general, resource-intensive generation and implantation of larger numbers of cells are used to compensate for the low post-transplantation cell-survival. Poor graft survival is often attributed to adverse biochemical, mechanical, and/or immunological stress that cells experience during and after implantation. To address these challenges, we developed a functionalized hyaluronic acid (HA)-based hydrogel for in vitro maturation and central nervous system (CNS) transplantation of human pluripotent stem cell (hPSC)-derived neural progenitors. Specifically, we functionalized the HA hydrogel with RGD and heparin (hep) via click-chemistry and tailored its stiffness to encourage neuronal maturation, survival, and long-term maintenance of the desired mDA phenotype. Importantly, approximately 5 times more hydrogel-encapsulated mDA neurons survived after transplantation in the rat striatum, compared to unencapsulated neurons harvested from commonly used 2D surfaces. This engineered biomaterial may therefore increase the therapeutic potential and reduce the manufacturing burden for successful neuronal implantation.

Scientific Abstract:
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